



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/734,460	12/11/2000	Jerome B. Zeldis	9516-018	5112

20583 7590 05/21/2003

PENNIE AND EDMONDS
1155 AVENUE OF THE AMERICAS
NEW YORK, NY 100362711

EXAMINER

EVANS, CHARESSE L

ART UNIT	PAPER NUMBER
----------	--------------

1615

DATE MAILED: 05/21/2003

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/734,460

Applicant(s)

ZELDIS, JEROME B.

Examiner

Charesse L. Evans

Art Unit

1615

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 February 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-31 and 44 is/are pending in the application.
- 4a) Of the above claim(s) 32-43 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-31 and 44 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Action Summary

Acknowledgement is made of the receipt of applicant's amendment and response, filed February 20, 2003.

Acknowledgement is made of the cancellation of claims 32-42, without prejudice.

Acknowledgment is made of the addition of new claims 43 and 44. However, claim 43 has been withdrawn, as it was not a part of the claim set as originally elected/presented. Applicant has elected, via original presentation, claims 1-31. Examination of claim 43 would require a new search.

Claims 1-31 and 44 are pending in this action.

Response to Arguments

Applicant's arguments filed February 20, 2003, have been fully considered but they are not persuasive. Applicant attempts to argue that there is no correlation between the disclosed congestive heart failure and atherosclerosis and stenosis. Examiner disagrees with this position. While all three conditions bare some differences in etymology, examiner asserts that it, indeed, would have been obvious to

one of ordinary skill in the art to modify the disclosed reference to apply to the treatment of atherosclerosis and stenosis. Congestive heart failure is related to the group of ischemic heart diseases that also include atherosclerosis and coronary artery disease. Examiner disagrees that at best, Mueller, provides an invitation to experiment. In all three conditions, there exists mechanical obstructions of the blood supply within the arterial cavity. Ischemic heart disease refers both to the presence of atherosclerotic coronary arteries and to the ultimate toll these conditions takes on the myocardium. Accordingly, it is the examiner's position that the Muller reference reads on applicant's claimed invention and that there exists a reasonable expectation of success by manipulating the referenced invention.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 4, 5, 7-10, 12-18, 20-23 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muller et al (US 5,635,517). The claims are directed to methods of preventing atherosclerosis and stenosis in a mammal comprising administering an effective amount of a TNF-alpha inhibitor, such as 1-oxo-2-(2,6-dioxopiperidin-3-yl)-4-aminoisoindoline.

Muller teaches a class of compounds used to decrease the levels of TNF-alpha. Specific compounds falling within the disclosed formula include 1-oxo-2-(2,6-dioxopiperidin-3-yl)-4-aminoisoindoline (column 7, lines 12). The referenced compounds are used to inhibit the undesirable effects of TNF-alpha and can be administered orally, rectally, or parenterally, alone or in combination with other therapeutic agents (column 4, lines 36-40). Oral dosage forms include tablets, capsules, dragees and similar shaped compressed pharmaceutical forms containing from 1 to 100mg of drug per unit dosage (column 6, lines 35-37). Please refer to Example 5 for an illustration of a preparation of tablets for chewing (column 9, Example 5). While the reference does not expressly teach applicant's claimed amounts, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 105 USPQ 233, 235 (CCPA 1955). It is the position of the examiner that these are limitations that would be routinely determined by one of ordinary skill in the art, through minimal experimentation, as being suitable, absent the presentation of some unusual and/or unexpected results. Absent a clear showing of criticality, the determination of the particular ranges and administration regiment is within the skill of the ordinary worker as part of the

process of normal optimization. The courts have held the “concentration limitations are obvious absent a showing of criticality.” Azko v. E.E. Pont de Nemours, 1 USPQ 2d 1704 (Fed. Cir. 1987).

The cited reference does not expressly teach utilizing this compound for the prevention of atherosclerosis or restenosis. However, it does teach a method of reducing tumor necrosis factor-alpha (TNF-alpha) levels with this compound. Excessive or unregulated TNF-alpha production has been implicated in a number of disease states. Therefore, decreasing TNF-alpha levels constitutes a valuable therapeutic strategy for the treatment of these inflammatory, infectious, immunological or malignant diseases such as congestive heart failure (column 3, lines 59-65). Congestive heart failure is related to the group of ischemic heart diseases that also include atherosclerosis and coronary artery disease. Accordingly, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the reference of Muller by formulating a pharmaceutical regimen that would decrease or mitigate factors that are known to cause damage and impairment to the muscle fibers that relate to the contractility of the heart muscle.

Allowable Subject Matter

Claims 11 and 24-31 are objected to as being dependent upon a rejected base claim, but may be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charesse L. Evans whose telephone number is

Application/Control Number: 09/734,460
Art Unit: 1615

Page 8

703-308-6400. The examiner can normally be reached on Monday -Thursday 7:00a - 4:30p; Alternating Friday 7:00a - 3:30p.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Charesse L. Evans
Examiner
Art Unit 1615

May 16, 2003


THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600